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(54) Title: COMPOSITION COMPRISING AN ANTIVIRAL OR ANTIBACTERIAL AGENT FOR PREVENTING TRANSMISSION OF DISEASES

(57) Abstract

Prophylactic compositions are disclosed which are effective in providing protection against the transmission of HIV infection during sexual activities. The compositions are based on synthetic saliva and incorporate a virucidal agent and preferably also an anti-bacterial agent.

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COMPOSITION COMPRISING AN ANTIVIRAL OR ANTIBACTERIAL AGENT FOR PREVENTING TRANSMISSION OF DISEASES

This invention relates to prophylactic compositions. Since the onset of the AIDS epidemic, there has been increasing emphasis on the promotion of so-called "safe sex". The surrounding educational efforts have largely concentrated on the promotion of the male condom which provides reasonable protection against transmission of HIV infection during conventional sexual activities.

Until recently, it was thought that oral sexual contacts did not produce any significant risk of transmission of the HIV virus, although there are already proven risks of transmission by oral contact in the case of other sexually-transmitted diseases such as gonorrhoea, herpes, warts, streptococcal infections and hepatitis B. Recent studies on monkeys, however, have shown that the related SIV virus can be transmitted orally.

It is, therefore, an object of the present invention to provide a prophylactic composition useful in reducing the transmission of sexually-transmitted diseases (STD) and transmission of diseases by orogenital sexual contact.

It is also an object of the present invention to provide a prophylactic composition which is useful also in reducing the risk of sexual transmission of pathogens during genital to genital and genital to manual sexual contact.

According to the present invention, therefore, there is provided a prophylactic composition effective in reducing the transmission of diseases by oral/genital, genital/genital or genital/manual contact, which comprises an active ingredient comprising an effective amount of an anti-viral or anti-bacterial agent in a liquid vehicle simulating natural saliva. In contrast with a normal mouth rinse, the

compositions of the invention can be formulated to have an effect extending over the duration of sexual contact. Thus, protection is provided for the necessary period required.

The compositions can be formulated so as to be effective against viral and bacterial STDs and other viruses and bacteria which might be transmitted in the course of sex, in particular oral sex, e.g. hepatitis B and human papilloma virus. A range of anti-viral agents exist and include, e.g. polyethylene glycol alkylphenylethers such as the nonyl and octyl homologues marketed under the trade names "Nonoxynol" and "Octoxynol" and di-isobutyl phenoxy polyethoxyethanol. These agents are non-ionic surfactants and are believed to owe their virucidal activity to their ability to disrupt viral membrane integrity. 'Nonoxynol' and 'Octoxynol' are manufactured respectively by Cilag Limited and ICI. In order to be effective in combating bacterial and viral agents within the mouth, the anti-bacterial or anti-viral agents should generally be present in an amount of from about 0.05 to 0.2 percent by weight, typically about 0.1 percent. For protection against HIV transmission, the anti-viral agent should be present in an amount of at least about 0.25%.

Anti-bacterial agents should preferably be included in the compositions of the invention along with the anti-viral agents. When used together with the anti-viral agent, the anti-bacterial agent should preferably be present in a concentration of at least 0.05%, preferably at 0.1%. Typical anti-bacterial agents include quaternary ammonium salts, such as benzalkonium chloride and cetrimide, imidazoles, such as metronidazole, clotrimazole, and miconazole, and antiseptics such as chlorhexidine acetate and gluconate.

The liquid vehicle in which the active agent is dissolved or dispersed comprises a viscous, slightly sticky material, having a viscosity and physical properties very similar to that of natural saliva. Such materials are currently available on the market as synthetic salivas and one commercial composition is available under the trade name "Saliva Orthana", manufactured by A. S. Orthana Kemisk Fabrik, Denmark. The composition is based on natural mucin extracted from pigs stomachs.

Other base materials suitable for the manufacture of synthetic salivas include cellulose derivatives, such as carboxymethyl cellulose. Commercially available synthetic salivas based on cellulose derivatives include 'Glandosane' and 'Salivace'. Synthetic salivas are currently prescribed for patients having eating, swallowing and speech difficulties, caused by a reduction in the production of natural salivas e.g. by cancer of the head and neck region. The paper by Vissink et al in International Journal of Oral Surgery, 1983, 12, pages 232 to 238, describes a typical saliva preparation and their use in the treatment of patients having depressed saliva production.

In accordance with the invention the anti-bacterial and/or anti-viral agent is dispersed in an effective amount in the synthetic saliva. The use of a vehicle simulating natural saliva as a carrier for the anti-bacterial and/or anti-viral agent is thought to aid greater adhesion of the active ingredient to the mucosa, whether in the mouth, vagina or anus. The resulting composition may be packaged in single dose sachets containing about 2.5 ml of the liquid prophylactic composition.

For example, just before sexual contact is anticipated, the passive partner can break the sachet and spread the synthetic saliva around the mouth. Other methods of dispensing the material include a water-soluble or chewable capsule or tablet. In the case of a tabletted composition, the ingredients will include hydrophilic materials or materials causing a rapid break-up of the tablet and the formation of a coating of synthetic saliva on the buccal and lingual surfaces. However, preferably, the compositions of the invention are packaged in an aerosol can or oral spray container. In the latter case, the spray container may be fitted with a metering pump so that the user sprays a measured amount of say 2-5 mls into the mouth.

For use of the prophylactic composition of the present invention in reducing transmission of diseases transmitted by genital/genital or genital/manual contact, alternative delivery/packaging systems may be preferred, in particular where the composition is to be applied, initially, to non-mucosal surfaces such as the hands.

One example of a typical formulation for the compositions of the invention is given below:-

Manufacturing Formula

The manufacturing formula for the preparation of 1 litre is:

Mucin (hog stomach) solution 4% in water		875 g
Xylitol		20 g
Methyl-4-hydroxybenzoate)	(Preservatives)	1 g
Benzalkonium chloride solution, 50%)		0.04 g
Ethylenediaminetetraacetic acid disodium salt x 2 H_2O	(Buffer)	0.5 g
Hydrogen peroxide solution, 35%	(Sterilising agent)	max. 0.86 g

Peppermint oil)	(Flavouring)	0.05 g
Spearmint oil)		0.05 g
Nonoxynol-9 (Cilag Ltd).		3 g
Purified water M		to 1 litre

In an alternative formulation, the mucin solution can be replaced by carboxymethyl cellulose in an amount of about 10 g of the solid material per litre of the made up composition.

CLAIMS:-

1. A prophylactic composition effective in reducing the transmission of diseases transmitted by oral/genital, genital/genital or genital/manual contact which comprises an active ingredient comprising an effective amount of an anti-bacterial or anti-viral agent in a vehicle simulating natural saliva.

2. A composition as claimed in claim 1 wherein the anti-viral agent is a poly(ethylene)glycol-alkylphenylether.

3. A composition as claimed in claim 2 wherein the anti-viral agent is nonylphenoxy-polyethoxy ethanol or octylphenoxy-polyethoxy ethanol.

4. A composition as claimed in any one of the preceding claims which contains both an anti-viral and an anti-bacterial agent.

5. A composition as claimed in any one of the preceding claims wherein the anti-viral agent is present in a concentration of at least 0.25% by weight.

6. A composition as claimed in any one of the preceding claims wherein the liquid vehicle comprises an aqueous solution or dispersion of a cellulose derivative or natural mucin.

7. A composition as claimed in claim 6 wherein the cellulose derivative is carboxymethyl cellulose.

8. A composition as claimed in any one of the preceding claims which is packaged as an aerosol or as an oral spray.

9. The use of a composition comprising an effective amount of an anti-bacterial anti-viral agent in a vehicle simulating natural saliva in the reduction of sexual transmission of diseases.

10. The use of an anti-bacterial or anti-viral agent and a vehicle simulating natural saliva in the preparation of a medicament for reducing the sexual transmission of diseases.

11. The use as claimed in claim 9 or claim 10 wherein the sexual transmission occurs through oral/genital contact.

12. The use as claimed in claim 9 or claim 10 wherein the sexual transmission occurs through genital/genital or genital/anal contact.

13. The use as claimed in any one of claims 9 to 12 wherein the anti-viral agent is a poly(ethylene)glycol-alkylphenylether; preferably nonylhenoxy-polyepoxy ethanol or octylphenoxy-polyethoxy ethanol.

14. The use as claimed in any one of claims 9 to 13 which contains both an anti-viral and an anti-bacterial agent.

15. The use as claimed in any one of claims 9 to 14 wherein the anti-viral agent is present in a concentration of at least 0.25% by weight.

16. The use as claimed in any one of claims 9 to 15 wherein the liquid vehicle comprises an aqueous solution or dispersion of a cellulose derivative or natural mucin.

17. The use as claimed in claim 16 wherein the cellulose derivative is caboxymethyl cellulose.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/00 A61K9/12 A61K47/38 A61K47/36 A61K31/765

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X	WO 95 08981 A (UNION CARBIDE CHEM PLASTIC ;BRODE GEORGE LEWIS (US); KREEGER RUSSE) 6 April 1995 see page 26, paragraph 2-4 ---	1-17
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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